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DEPARTMENT OF THE ARMY
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THE PRODUCTION OF MORGAN'S TOXICOINFECTION IN MONKEYS IN RELATION TO ACUTE RADIATION SICKNESS

- USSR -

[Following is a translation of an article by L. A. Yakovleva, B. A. Lapin and S. M. Peherman in the Russian language periodical Medical Radiology, vol. 7, no 8, August 1962, pages 65-68.]

At the present time it is well established that a single, massive irradiation significantly decreases the animal organism's resistance to various agents of infection, both bacterial and virus. The investigations of native and foreign writers were presented in the recently published monographs of V. L. Troitskiy and M. A. Tumanyan (1958), O. P. Peterson with co-authors (1961). Similar research on these problems in relation to monkeys has been very scarce. For example, M. A. Tumanyan, in experiments on monkeys, noted an abrupt increase in their sensitivity to dysentery during irradiation at lethal and sub-lethal doses of ionizing irradiation.

We obtained similar results in studying the course of Breslau's paratyphoid fever in relation to irradiation at sub-lethal dosage. Z. K. Stasilevich, studying factors determining the natural resistance of monkeys to Salmonellas and coli-enteritis, established that during sub-lethal dose irradiation there is an increase in susceptibility of animals to coli-enterites and paratyphoid fever B, as well as a significant increase in the severity of these infections and Heidelberg's paratyphoid fever. Dysenteric and paratyphoid fever agents, however, are considered highly pathogenic for monkeys. In maintaining these animals in cages, without any experimental interventions, one can encounter the appearance of these infectionary processes in them; their occurrence often assumes the character of an epidemic outbreak. In a number of cases it is also possible to produce these infections in monkeys artificially.

We considered it useful to clarify whether susceptibility [illegible] and the course of the illness becomes more severe only in the [illegible] listed above (having a relatively wide "spontaneous" [illegible] monkeys and artificially induced in them), or [illegible]

larities/spread according to illnesses produced by pathogenic stimuli. With this aim we dwelt on the experiment of producing Morgan's toxicoinfection whose stimulus, being conditionally pathogenic for monkeys, can often be found in the feces of healthy animals. Apparently monkeys rarely become ill from Morgan's toxicoinfection. In isolated cases, however, diarrhetic monkeys excrete Morgan's bacillus (Levell, Hamerton).

In the past 7 years, monkeys of the Sukhumskiy nursery were found to have Morgan's toxicoinfection, confirmed bacteriologically, only 3 times. In this case, the disease had the character of an epidemic outbreak; 3 young monkeys less than a year old who were on artificial feeding became ill and died within several days. In relation to all autopsies on monkeys (1600) conducted during this period, death from Morgan's toxicoinfection was responsible only for 0.18%.

The clinical and pathomorphological picture in the dead animals was characterized by the development of a severe catarrhal-hemorrhagic gastroenteritis. This was accompanied by swelling of the mesenterial lymphatic nodes and enlargement of Payer's patches of the ileum. Enlargment of the intestinal lymphatic apparatus and that of the mesentery was associated with hyperemia, edema, and proliferation of lymphoid elements in lymphatic formations.

We used young Rhesus monkeys of an average age from ½ to 1½ years. Contamination was conducted according to the same technique used in the investigation of experimental paratyphoid infection of monkeys. The monkeys were contaminated by mouth on an empty stomach by daily agar culture in quantities of 30-50 mlrd. microbe bodies following preparatory induction, one hour prior to contamination, of 3-5 ml bull bile (depending on the age of the animal).

The attempt to infect 10 monkeys without prior irradiation was not successful. The animals remained healthy, according to clinical findings and blood indicators. For some time following contamination (from 3 to 16 days in different animals), however, there were large quantities of Morgan's bacteria in the fecal matter. Venous blood samples remained sterile. Starting with the second week the blood of all infected monkeys showed anti-bodies to Morgan's bacteria in titers of 1:200; and by the 15-16th day — in titers of 1:300. Later we observed a decrease in anti-body titer.

Infection of 7 monkeys under the same conditions with preceding irradiation gave somewhat distinctive results. The animals were subjected to irradiation in 300 r doses on the twin RUM-3 apparatus 2-3 days prior to infection (voltage: 180 kV; current: 15 mA; dosage strength: 17 r/hour). In experiments we conducted earlier, irradiation of monkeys in doses of 250-300 r produces a very light form of radiation sickness which is clinically characterized primarily by the development of short-term, superficial leukopenia (2,500-3,000 leukocytes/1 mm3 of blood).

Out of 7 irradiated and infected monkeys, 7 became ill. The illness was characterized by the appearance of a watery, fetid stool from the 2nd day following irradiation; the stool was sometimes mixed with mucus. In all the sick monkeys we observed listlessness, loss of appetite in various degrees. The diarrhea was accompanied by significant increase

in the ESR (from 18 to 46 mm/hour). The illness was accompanied by a moderate leukopenia (2,400-1,800 leukocytes/1 mm³). In four seriously ill animals (Sima, Perez, Shayim, Polchok), by the 3-4th day, one could already observe the appearance of significant emicosis in the form of a severe rolling back of the eyes and decrease in skin turger. In 2 of these animals (Polchok and Sima) repeated vomiting was observed. On rib cage auscultation, moist rales were heard in 3 animals. The duration of the illness varied. In 2 mildly sick animals (Shura and Yorkin) the mild diarrhea (without any disturbance of the general state of the animals, and with ESR increase to 18 mm/hour) continued only 3 days. In the two monkeys who survived the illness with severe diarrhea, the illness lasted a relatively short time -- 7 and 13 days. Fecal bacteria in all animals was observed a relatively short time -- from 2 to 6 days.

The agglutination reaction from the blood serum of all irradiated animals 2½ weeks following infection gave no positive result. Two monkeys from this group (Sima and Shayim) died on the 3rd and 7th day of the illness, corresponding to the 5th and 10th day following irradiation.

On pathologoanatomical autopsy of these animals, Morgan's bacteria was found in the contents of the stomach, and small and large intestine. In one case (Sima), the microbe was also found in lung tissue. In the monkey who died on the 3rd day of illness, we observed catarrhal inflammation of the mucous membrane of the small and large intestine, accompanied by severe swelling of intestinal loops. The mucous membrane was pink and swollen throughout. Edema and hyperemia of the mucous and submucous intestinal layers were observed. Edematous villi of the small intestine were usually deprived of epithelial covering. The contents of the small and large intestine were watery. Intestinal inflammation was not accompanied by noticeable hyperplasia of the spleen and mesenterial lymph nodes. The lymph nodes were observed to have significant edema and hyperemia with severe dilatation of the sinuses. In sinus lumens we find a large quantity of microphages in whose protoplasm there are often erythrocytes, brown pigment, and cell fragments. In some areas of the sinus lumen we found the fine network of fibrin. The quantity of cells in the cortical layer of the mesenterial and peripheral nodes was somewhat decreased; this did not, however, appear in the form of significant wasting away of lymphoid tissue. Light centers were not numerous, and were of small sizes. There was often cell degeneration with rhexis of the nucleus. The spleen was small; moderately firm, with a well-marked network of trabeculae and small follicles. The quantity of lymphocytes appeared significantly decreased. Blood vessels were usually distended. Small hemorrhages were encountered. This monkey was also suffering from focal pneumonia having a very mixed morphological character. At the same time that alveolar groups were observed filled with leukocytic exudate, alveoli were encountered with serous fluid in the lumen containing various quantities of macrophages. In some areas the alveoli were almost completely full of erythrocytes, and sometimes with fibrin. The process had the distinctive character of bronchopneumonia with leukocytic infiltration of bronchial walls and with serous-leukocytic exudate filling lumens of the bronchi. Other internal organs presented a picture

of moderate hyperemia. Under the endocardium of the left ventricle, there were a few hemorrhages.

In the second case, where the monkey died on the 7th day of illness, pathomorphological investigation showed severe gastroenteritis with severe edema of the mucous, sub-mucous, and in some places of the serous layer, as well as the appearance of a large number of hemorrhages in the stomach and along the course of the small intestine. The mucous membrane of the stomach showed small necroses. The contents of the small and large intestine were watery with pinkish-gray small flakes. In microscopic section, follicles were not distinguished.

In microscopic investigation, significant hyperemia of the organ was observed with blood overflow in the sinuses. Follicles were small. The quantity of lymphocytes in them was noticeably reduced. Light centers in follicles were found relatively infrequently. Occasionally we found here an accumulation of protein exudate. We had similar findings in the mesenterial lymph nodes where the number of lymphocytes was also clearly reduced. We found, just as in the monkey who had died on the 3rd day, that the nodes had severe distension of sinuses with an accumulation of a large number of macrophages. We very often observed erythrocytes in macrophage protoplasm, and less often — clumps of brown pigment.

These observations are evidence that the stimulus for Morgan's toxicoinfection, being for Rhesus monkeys conditionally pathogenic and not inducing in artificial infection the appearance of an infectionary process, on x-ray irradiation of these animals at sub-lethal doses, produces the development of a severe process of infection concluding in a number of cases with the animals' death. The illness, appearing in relation to irradiation, does not differ as a whole from the spontaneously appearing illness, and has the character of severe gastroenteritis. Irradiation, however, imposes its mark on the morphological manifestation of this illness in the form of the development of moderate atrophic phenomena in the spleen and intestinal lymphatic apparatus.

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